Advances in Progressive MS Research

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Overview

1. What is progressive MS?

2. Key advances in progressive MS research

3. What is your Society doing to find solutions for people living with all forms of MS?
What is Progressive MS?

- **Neurologist**
  - Secondary-progressive MS course
  - Graph showing degree of disability over time with relapses.

- **Radiologist**
  - MRI scans showing brain at baseline, month 6, month 12, and month 18.

- **Pathologist**
  - Microscopic images of tissue samples labeled A and B.

- **Physiatrist**
  - Image of a physiatrist examining a patient's leg.

- **Person with MS**
  - Image of a person with MS sitting in a wheelchair outside a busy street.
Relapsing-remitting MS

85% at onset

Primary Progressive MS

10-15%

Progressive-relapsing MS

5-10%

Secondary Progressive MS

~50% of RRMS develop SPMS
Progression: Gradual Worsening of Symptoms and Disability

Two main types of progressive MS:

• Most common is secondary-progressive MS – people who first experience relapses and remissions, then transition to gradual worsening of disability

• Less common is primary-progressive MS – gradual worsening from onset without relapses or remissions.
How is it Different from Relapsing MS?
Progression: What We Know

- Progression often occurs early, even without symptoms
- People progress at different rates – some rapidly, some slowly, and the rate is unpredictable
- Primary-progressive MS often takes longer to diagnose, after nervous system injury leads to first symptoms
- Progressive disability appears to reflect injury to nerves
Why Aren’t There More Treatments for Progressive MS?

- Virtually every therapy approved for relapsing MS has been tested in progressive MS.
- Trials in relapsing MS often count relapses or MRI lesions; Progression is not easily measured using MRI.
- Without such quick readouts for progressive MS, it’s more challenging to track success of therapies.
Possible Mechanisms of Nerve Degeneration in MS

- **Dysfunction in myelin repair**
  - May deny the neurons survival signals
  - Leaves the neurons vulnerable

- **Neuronal cell damage induced by:**
  - Excitotoxicity
  - Oxidative stress
  - Loss of nerve cell support factors/receptors
  - Energy failure
Normal White Matter
Remyelinated Lesion - Shadow Plaque
Key advances in progressive MS research
Historic Advances Funded by Society

• First results showing that aerobic exercise could fight MS fatigue, changing doctors’ age-old advice to “take it easy”
• Discovery that human adult brains have replacement cells for myelin, and showed that transplanting those cells could restore function in mice
• Research on cognition problems in MS as well as rehabilitation strategies to address them
• Development of a tool that measures improvements in quality of life
• Early trials that led to approved medicine to improve walking in MS
Recent Advances: Promoting Natural Myelin Repair with Anti-LINGO

- LINGO-1 inhibits remyelination
- Anti-LINGO-1 promotes remyelination in an MS-like disease in mice
- Shown to be safe in early human trials
- Currently in a phase II trials in MS and optic neuritis

Mi, et al., Nature Medicine, 2007; 13(10):1228
Recent Advances: Repurposing FDA-Approved Benztropine to Promote Repair

A regenerative approach to the treatment of multiple sclerosis

Vishal A. Deshmukh1, Virginia Tardif1, Costas A. Lymriotis4, Chelsea C. Green1, Bilal Kermani3, Hyung Joong Kim3, Krishnan Padmanabhan3, Jonathan G. Swoboda1, Insha Ahmed1, Toru Kondo2, Fred H. Gage1, Angelos N. TheoPhilopoulos3, Brian R. Lawson1, Peter G. Schultz1,* & Luke I. Lairson1,*
Recent Advances: Simvastatin (Zocor) Trial (MS-STAT) in SPMS

- Jeremy Chataway - University College London
- High dose simvastatin (80 mg)
- 140 people with established SPMS
- 50% decrease in brain atrophy
- Significant Improvement in disability
Recent Advances: Society-Supported Exercise and Rehabilitation Research

• Progressive resistance weight training improves walking and quality of life
• Balance/eye movement training improves fatigue and reduces disability due to dizziness or disequilibrium
• Cognitive rehabilitation improves learning and memory lasting at least 6 months
Recent Advances: Society-Supported Stem Cell Therapy Studies

• University of Rochester team transplanted stem cells derived from human skin into mice. The cells became myelin-making cells that quickly formed new myelin.

• Researchers in Milan, Italy have transplanted myelin-making cells derived from mouse skin stem cells into the spinal cord of mice, which promoted recovery of MS-like symptoms.
What is your Society doing to find solutions for people living with progressive MS?
Finding Solutions for people with MS is Our Highest Priority

- Research is essential to finding solutions that change lives
- Fueling research through increased investment - $50 mil in 2014

Our approach is comprehensive and we collaborate worldwide

- Pursue all promising paths, wherever they exist
- Three priority areas: Progressive MS, Nervous System Repair (including Myelin Repair), Wellness/Lifestyle
- Remain nimble to seize promising new opportunities
Society Research Priorities in Progressive MS

• Accelerate clinical trials in progressive MS
• Understand what drives progression and nervous system damage and find new therapies to treat it
• Find better rehabilitation and treatments for symptoms to improve quality of life
• Discover how to repair the nervous system to restore function
Driving Solutions: Accelerating Clinical Trials in Progressive MS

- MS Outcome Assessments Consortium (MSOAC) is working on a new measure of disability to be recognized by the FDA and the European Medicines Agency to speed new therapies for MS
- Other efforts focus on high-tech imaging tools to better measure nerve tissue damage and assess nerve protection and repair without having to wait years to observe a person’s disease progression
- Designing new ways of conducting clinical trials and better outcome measures and biomarkers to speed up the testing of promising repair strategies
Driving Solutions: Trials of neuroprotection as proof of concept for stopping MS progression

– Lipoic acid – antioxidant may help block nerve fiber damage in MS
– Phenytoin – reduces entry of sodium into nerve fibers
– MS-SMART trial – testing 3 therapies that may have nerve-protecting properties in SPMS
– Ibudilast – collaborative trial in 250 people with progressive MS
Driving Solutions: Understand What Drives Progression

• Exploring mechanisms that cause nervous system injury to expose potential therapeutic targets along the injury pathways to stop the damage

• Using advanced imaging and laboratory studies to define and track MS disease activity, MS lesions, and atrophy in the brain and spinal cord

• Epidemiology studies designed to identify factors that contribute to the risk of MS progression
Driving Solutions: Rehabilitation Research
-- Funding >30 projects testing ways to help people live their best lives

- New strategies for balance control
- Methods for improving lung function
- Cycling regimens to reduce spasticity
- Exercise regimens for people with advanced MS
- Home-based exercise to improve mobility and cardiovascular health
- New strategies for improving cognitive function and psychosocial wellness
Driving Solutions: Rehabilitation Research - **Training**

- Rehabilitation = interventions to help people achieve physical, psychological, social and vocational potential.
- To convince doctors/insurers of their worth, need evidence from well-conducted studies.
- Society offers fellowships to support mentors who train professionals in how to conduct rehabilitation research studies.
- Launched in 2006, this program’s trainees are young researchers driving progress today.
Driving Solutions: Nervous System Repair

• Society’s Fast Forward collaborating with EMD Serono to identify/validate new targets in repair and protection
• Improving clinical trial design to test repair strategies (Int’l Advisory Committee on Clinical Trials in MS)
• Exploring repair potential of different types of stem cells in pre-clinical models
• Focusing on high-tech imaging to speed up tracking of damage/repair
An expanding alliance of MS organizations from around the world

Mission
To expedite the development of therapies for effective disease modification and symptom management in progressive MS

www.endprogressivems.org